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Journal of the Chinese Medical Association 77 (2014) 273–274

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## Editorial

# Sowing the seeds of health: Is the era of food prescriptions coming?



In the past few decades, there is an astonishing amount of accumulated evidence that indicates that natural compounds extracted from plants exert—at least *in vitro*—significant effects against many pathological conditions. The term “phytochemical” has been introduced, which is defined as bioactive chemicals in fruits, vegetables, grains, and various plants that may provide health benefits.<sup>1</sup> A mechanism for this is that phytochemicals provide antioxidant defenses that ameliorate DNA oxidation and affect cellular signal transduction pathways controlling cell proliferation and apoptosis.<sup>1</sup> In human studies, consuming fruits and vegetables at greater than the average amount is associated with the reduced risk of diseases such as cardiovascular disease and malignancy.<sup>2</sup> Another study reports that the sum of different flavonoid intake (e.g., quercetin, myricetin, kaempferol, luteolin, and ficetin) was inversely correlated with plasma total cholesterol concentration and low-density lipoprotein cholesterol concentration.<sup>3</sup>

One remarkable advantage of using natural products as pharmaceuticals is their relatively low toxicity or lack of toxicity within a wide range of dosages, which contributes to a better success rate on entering into a Phase I trial, compared to conventional chemicals (25% vs. 6%, respectively).<sup>4</sup> Therefore, it can be speculated whether it is possible to actually control diseases with phytochemicals. Several ongoing concerns should lead investigators to proceed with caution as relevant data are considered. A concern is the extent to which success in animal studies can be applied to clinical practice.

Experiments on animals provide crucial background and necessary information, which enhance the execution and efficacy of clinical trials. However, a compound or ingredient that is effective for animals may not work in human patients. The most straightforward but often overlooked factor can be the lack of appropriate dose extrapolation from animal experiments to human application. The dose calculation should not be based merely on body weight. The Food and Drug Administration of the United States has actually suggested that the extrapolation of animal dose to human dose is correctly performed only through normalization to body surface area.<sup>5</sup>

The second concern is that the yield of phytochemicals from plants can be limited because of technical issues or

because the amount of the available plant is restricted by special cultivation requirements. To solve these potential problems, *in vitro* reconstruction and biosynthesis have been developed.<sup>6</sup>

A third concern is the low bioavailability of some phytochemicals. In fact, some antioxidants do not appear to have consistent benefits in large-scale human studies.<sup>7</sup> In one clinical trial, the incidence of malignant cancers was unchanged in patients taking a  $\beta$ -carotene supplement.<sup>8</sup> The isolated pure compound either loses its bioactivity or may not provide the anticipated benefit when delivered in food form. For instance, different species of fruits have a variety of phytochemical profiles.<sup>9</sup> The additive and synergistic effects of phytochemicals may be pivotal factors that account for their potent antioxidant activities. A recent survey revealed that apple phytochemical extracts and quercetin 3- $\beta$ -D-glucoside used in combination exert a synergistic effect against MCF-7 human breast cancer cell proliferation.<sup>10</sup> This therefore suggests that, although routine clinical prescription of a single phytochemical is becoming more feasible as a way to prevent or cure disease, people should obtain phytochemicals from a wide variety of fruits, vegetables, and whole grains for balanced health benefits. It is indeed inevitable that multiple intrinsic and extrinsic factors such as storage time, genetic factors, physiological factors, and the impact of cooking have strong influences on the content and bioactivities of phytochemicals among different kinds of foods.<sup>11,12</sup>

In this issue, two remarkable studies that focus on the effects of phytochemicals are presented. Tarik Mohammed Chaouche et al.<sup>13</sup> revealed the total phenolic, flavonoid, and tannin contents of three Algerian medicinal plants (*Echium pycnanthum* Pomel, *Haloxylon articulatum* Boiss, and *Solenostemma oleifolium* Bull. & Bruce). They found that these South Algerian plants possess high *in vitro* antioxidant potency, which may be feasible for applied medicinal purposes in humans.<sup>13</sup> In another study, Ai-Ren Zuo et al.<sup>14</sup> examined the hepatoprotective effects of phloretin and phloretin isonicotinyl hydrazone (PIH) on D-galactosamine-induced acute liver damage in mice. The results revealed that phloretin or PIH administration significantly ameliorated serum biochemistry abnormalities and histological changes in acute liver damage. Phloretin and PIH also exhibited antioxidant effects

on lipid peroxidation in rat liver mitochondria, free radical scavenging activity *in vitro*, and supercoiled pBR322 plasmid DNA. Furthermore, a good antityrosinase activity was also present. Phloretin is a type of apple-derived flavonoid that has antioxidant properties. Phloretin isonicotinyl hydrazone is a novel compound synthesized by the same group; it exerts a higher level of antioxidant activity than phloretin.<sup>15</sup> These investigations show the characteristics and benefits of various phytochemicals *in vitro* and in animal models. In fact, human trials are anticipated to ascertain their clinical potential.

### Conflicts of interest

The author declares that there are no conflicts of interest related to the subject matter or materials discussed in this article.

### References

1. Liu RH. Potential synergy of phytochemicals in cancer prevention: mechanism of action. *J Nutr* 2004;**134**:3479S–85S.
2. Genkinger JM, Platz EA, Hoffman SC, Comstock GW, Helzlsouer KJ. Fruit, vegetable, and antioxidant intake and all-cause, cancer, and cardiovascular disease mortality in a community-dwelling population in Washington County, Maryland. *Am J Epidemiol* 2004;**160**:1223–33.
3. Arai Y, Watanabe S, Kimira M, Shimoi K, Mochizuki R, Kinai N. Dietary intakes of flavonols, flavones and isoflavones by Japanese women and the inverse correlation between quercetin intake and plasma LDL cholesterol concentration. *J Nutr* 2000;**131**:2243–50.
4. Schmid RD. *Pocket guide to biotechnology and genetic engineering*. Cambridge, MA: Weinheim; 2003.
5. Center for Drug Evaluation and Research. Center for Biologics Evaluation and Research. *Estimating the safe starting dose in clinical trials for therapeutics in adult healthy volunteers*. Rockville, MD, U.S.: Food and Drug Administration; 2002.
6. Mora-Palea M, Sanchez-Rodriguez SP, Linhardt RJ, Dordicka JS, Koffas MAG. Metabolic engineering and *in vitro* biosynthesis of phytochemicals and non-natural analogues. *Plant Sci* 2013;**210**:10–24.
7. Yusuf S, Dagenais G, Pogue J, Bosch J, Sleight P. Vitamin E supplementation and cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med* 2000;**342**:154–60.
8. Hennekens CH, Buring JE, Manson JE, Stampfer M, Rosner B. Lack of effect of longterm supplementation with  $\beta$ -carotene on the incidence of malignant neoplasms and cardiovascular disease. *N Engl J Med* 1996;**334**:1145–9.
9. Sun J, Chu YF, Wu X, Liu RH. Antioxidant and antiproliferative activities of fruits. *J Agric Food Chem* 2002;**50**:7449–54.
10. Yang J, Liu RH. Synergistic effect of apple extracts and quercetin 3- $\beta$ -D-glucoside combination on antiproliferative activity in MCF-7 human breast cancer cells *in vitro*. *J Agric Food Chem* 2009;**57**:8581–6.
11. Ksouri R, Megdiche W, Falleh H, Trabelsi N, Boulaaba M, Smaoui A, et al. Influence of biological, environmental and technical factors on phenolic content and antioxidant activities of Tunisian halophytes. *C R Biol* 2008;**331**:865–73.
12. Palermo M, Pellegrini N, Fogliano V. The effect of cooking on the phytochemical content of vegetables. *J Sci Food Agric* 2014;**94**:1057–70.
13. Chaouche TM, Haddouchi F, Ksouri R, Atik-Bekkara F. Evaluation of antioxidant activity of hydromethanolic extracts of some medicinal species from South Algeria. *J Chin Med Assoc* 2014;**77**:302–7.
14. Zuo AR, Yu YY, Shu QL, Zheng LX, Wang XM, Peng SH, et al. Hepatoprotective effects and antioxidant, antityrosinase activities of phloretin and phloretin isonicotinyl hydrazone. *J Chin Med Assoc* 2014;**77**:290–301.
15. Zuo AR, Yu YY, Li J, Cao SW. Study on the relation of structure and antioxidant activity of isorhamnetin, quercetin, phloretin, silybin and phloretin isonicotinyl hydrazone. *Free Rad Antiox* 2011;**1**:39–47.

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